II. REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. Claims 1-30 are currently pending and remain at issue. This response is timely filed as it is accompanied by a petition for an extension of time to file in the third month and the required fee.

In paragraph one of the official action, the examiner objected to claims 5-30 under 37 C.F.R. §1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Accordingly, the examiner did not examine the claims further. The applicants have amended claims 2-25 to remove multiple dependencies and place in proper form. Solely for the purpose of expediting prosecution, and without prejudice to the applicants right to seek broader claims in a continuing application, and not for any reasons related to patentability, the applicants have canceled claims 25-30. New claim 31 is directed to a method according to claim 16, wherein R1 and R2 are further selected from the group consisting of fluorine, chlorine, bromine, iodine, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, or phenyl groups. New claim 32 is directed to a method according to claim 22, wherein the electron donating moiety is defined in claim 15. New claim 33 is directed to a method according to claim 32, wherein the reporter group is a mass marker and the method further comprises cleaving off the mass marker in a mass spectrometer. New claims 34 and 35 further define the metal ions used in the method of claim 16. Support for new claims 31-33 can be found throughout the specification, for example, originally filed claims 2, 12, 13, 23, and 24.

The applicants do not intend by these or any amendments to abandon the subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Patentability Remarks

Rejection Pursuant 35 U.S.C. §112, First Paragraph

In paragraph 3 of the official action, the examiner rejected claims 1-4 under 35 U.S.C. §112, first paragraph, for allegedly failing to comply with the enablement requirement. Specifically, the examiner alleged that no guidance is provided by the specification for the preparation of the instantly claimed compounds with the chemical

formula (I). The examiner asserted no working examples are provided for the synthesis of the instantly claimed compounds and thus undue experimentation would be required by one of ordinary skill in the art to make the claimed compounds of the formula (I). The applicants respectfully traverse.

The applicants submit the specification provides specific examples of the four constituent groups N, M, R1 and R2, which are bounded to a central silicon atom. Specifically, the passage from line 28, page 4 to line 4, page 5 describes examples of nucleic acids that can comprise the analyte. Examples of the substituents R1 and R2 are provided on page 5, lines 5-22. A number of different examples of mass-markers are provided on pages 6-8 of the specification. All of the groups referred to in the description and claims of the four constituent groups (N, M, R1 and R2) of the claimed compounds are common groups in organic chemistry and their properties are well understood by persons skilled in the field to enable them to generate compounds of the general formula (I).

The applicants further submit that it is important that the mass-marker or the nucleic acid section of the compound be cleaved from the silicon atom and not the other substituents attached to the atom (*i.e.*, R1 and R2). Selecting the disclosed groups of R1 and R2 will allow either the mass-marker or the nucleic acid to be cleaved from the silicon atom because the disclosed groups within the disclosed list of suitable mass-marker and nucleic acids are better leaving groups than R1 and R2. The specification is enabling because it teaches that selecting groups of R1 and R2 will create greater bond energy with Si than the bond energy of those substituents of N and/or M. Understanding that the substituents of N and/or M must be better leaving groups than R1 and R2 is well without in abilities of those with ordinary skill in the art and would not require undue experimentation. As stated above, examples of groups suitable for N, M, R1 and R2 are given in the description.

Finally, the applicants submit that the example of the present specification demonstrates the fact that the reaction mechanism actually works, *i.e.* a working example of the chemistry utilized by the presently claimed molecule. As stated previously, this chemistry is well known in the field of endeavor. In view of the foregoing remarks, the applicants respectfully submit the rejection of claims 1-4 under 35 U.S.C. §112, first paragraph, has been overcome and request the withdrawal of the same.

Rejection Pursuant 35 U.S.C. §112, Second Paragraph

In paragraph 5 of the official action, the examiner rejected claims 1-4 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Specifically, the examiner alleged the phrases "M comprises" and "N comprises" render all claims, wherein variables "M" and "N" are not distinctly described, indefinite to one of ordinary skill in the art. In addition, the examiner asserted the phrase "wherein the nucleotide or oligonucleotide is nature, or is modified" and the term "substituted" render the claims indefinite. The examiner further alleged that in absence of distinct modifications to the chemical core claimed or distinct language to describe the structural modifications or the chemical names of modified/substituted compounds of this invention, the identity of said modified/substituted compounds would be difficult to describe.

The applicants submit the M and N groups are distinctly described in the specification. As stated above, the description provides specific examples of the four constituent groups N, M, R1 and R2 that are bonded to the central silicon atom. In particular, examples of nucleic acids are given in the paragraphs bridging pages 4 and 5, examples of substituents R1 and R2 are given on page 5, lines 5-22, and examples of mass-markers are given on pages 6-8 of the description.

With regard to the phrases "wherein the nucleotides or oligonucleotide is nature, or is modified" and the term "substituted," the applicants submit that in lieu of the examples of mass markers, N groups, R1 groups, and R2 groups provided in the description, one of skill in the art would be able to determine which substitutions or modifications would be suitable for the N and M groups. Accordingly, the phrases "wherein the nucleotides or oligonucleotide is nature, or is modified" and the term "substituted" are particularly pointed out in the claims because one of skill in the art would understand which substitutions and/or modifications would have to be made to the N and M groups due to the teachings of the disclosure. In view of the foregoing remarks, the applicants submit the rejection of claims 1-4 under 35 U.S.C. §112, second paragraph, has been overcome and should be withdrawn.

Rejection Pursuant 35 U.S.C. §102

In paragraph 7 of the official action, the examiner rejected claims 1-4 under 35 U.S.C. §102(b) as allegedly being anticipated by Lawson *et al., J. of the American Chemical Society* 93:1014-1023 (1971). Specifically, the examiner alleged the term "mass marker" has been interpreted broadly to mean any moiety having a mass detectable by any means known in the art at the time of invention. The examiner further asserted the instantly claimed compounds of formula (I) are anticipated by Lawson *et al.* because Lawson *et al.* discloses trimethylsilyl derivatives of nucleotides corresponding to instantly claimed formula (I) wherein N is a nucleotide and R1, R2, and M are methyl groups.

The applicants submit that the particular compound claimed in claim 1 is novel because the R1-Si-R2 group acts as a linker between a mass-marker and a nucleic acid. It has been found that the Si linker is particularly sensitive to the type of cleavage claimed in claim 1 and illustrated in Figure 1. When reacting with an electron donating moiety, this arrangement allows the mass-marker or the nucleic acid to be cleaved first in preference to the R1 and R2. This is in contrast to prior art arrangements wherein the mass-marker was attached to the nucleic acid, and thus neither the mass-marker or the nucleic acid where cleaved preferentially.

The applicants further submit that by allowing the nucleic acid or mass marker group to be cleaved first by an electron donating moiety, the product species containing the nucleic acid are neutral (see Figure 1 of the present application) and is thus not detected in the mass spectrum (*i.e.* these product species' are not mass-marked), while the charged mass-marker is detectable in the mass spectrum (*i.e.* these product species are mass-marked (see Figure 1)). This leads to a much cleaner mass spectrum than that obtained by a charged product nucleic acid species which would have occurred according to prior art arrangements such as Lawson *et al.* (see below).

In addition, the applicants further submit in reviewing Lawson *et al.*, it would appear that in order for the disclosed compounds to fall within the formula (I) of claim 1, then M, R1 and R2 must all be the same (*i.e.* methylene groups). The applicants submit that R1, R2 and M would show no relative differences in their susceptibility to cleavage. Accordingly, the structures recited in Lawson *et al.* would not satisfy the functional requirements of claim 1 insofar as **claim 1 requires cleavage of M in preference to R1 and R2.**

In addition, the applicants respectfully submit that the examiner has misconstrued the meaning of the term mass-marker as it is used in claim 1. The examiner has interpreted the term "mass-marker" to mean any moiety having a mass detectable **by any means** known in the art at the time of the invention. This, however, is incorrect. First, the term "mass-marker" means **any moiety** which is detectable by mass spectrometry rather than by any means. Secondly, in terms of the wording of claim 1, the term "mass-marker" must mean any moiety which is detectable by mass spectrometry after the compound **has reacted** with an electron donating moiety. As such, the species M in claim 1 must be any moiety which is detectable by mass spectrometry after the reaction of the claimed compound with an electron donating moiety.

In view of the aforementioned construction of claim 1, it is clear that Lawson *et al.* does not disclose a mass-marker at all. The methyl group identified by the examiner cannot be a "mass-marker" within the meaning of the term in claim 1. The reaction of a compound of the type (CH3)3Si-(Nucleic acid) with an electron donating moiety would result in wholly neutral product species' none of which are detectable. Thus, all species would have to be further processed to produce charged fragments, and all the fragments would have to be detected. This would result in a very messy spectrum which would be difficult to interpret.

Finally, there is no suggestion in Lawson *et al.* to carry out the cleavage as specified in claim 1, which results in a neutral nucleic acid product species. In contrast, Lawson *et al.* discloses compounds which cleave at a P-O-C linkage to produce a charged nucleic acid species which is detectable in the mass-spectrum. There is absolutely no disclosure or suggestion in Lawson *et al.* of providing a compound in which a moiety is bound by an Si linker to a nucleic acid, wherein the moiety is detectable in a mass spectrometer after the reaction with an electron donating moiety.

III. CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action such action is hereby solicited. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number listed below.

Respectfully submitted,
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